Hartley et al., 1996; Madshus and Stenmark, 1992), for example (Ribosome inactivating proteins) RIPs which enter the cytosol and are among the most potent cytotoxins known. Ribosome-inactivation is achieved in all cases through the cleavage of an N-glycosidic bond between ribose and a specific adenine residue in the universally conserved sequence 5'-AGUACGA*GAGGA-3' (where A* indicates the target adenine) (SEQ ID NO: 164) located 250-400nt from the 3' end of 23S/25S/28S rRNAs (Endo and Tsurugi, 1987), (Hartley et al., 1996). Ribosomes depurinated in this manner are unable to bind the EF-2/GTP complex and protein synthesis is blocked at the translocation step (Montanaro et al., 1975). A single RIP molecule is able to depurinate 1000-2000 mammalian cell ribosomes per min under physiological conditions (Eiklid et al., 1980; Endo and Tsurugi, 1988). --

Please replace the paragraph beginning at page 17, line 6, with the following amended paragraph.

-- In the constructs according to the invention, the antibody is preferably fused to a complete sequence of a toxic agent or a part thereof which still has activity, or which is still functionally active. Also, the chimeric protein may be encoded by nucleotide sequences on one or more constructs and may be assembled *in vivo* by the plant or expression organisms protein assembly and translation machinery. The

chimeric protein can also be obtained by biochemical assembly or *in vitro* or *in vivo* assembly of the chimeric immunotoxin subunits using the cells endogenous protein assembly machinery. The antibody, antibodies or fragments thereof are fused directly to the toxic agent or linked by a flexible spacer which does not interfere with the structure or function of the two proteins. Such flexible linkers include copies of the (Glycine-Glycine- Glycine- Glycine-Serine)$_n$ linker (SEQ ID NO: 165 - also referred to as Gly_4Ser), where n is 1 to 4 or more copies of the linker unit, the Genex 212 and 218 linker and the flexible linker peptide of *Trichoderma reesi* cellobiohydrolase I (CBHI) (Turner et al., 1997), (Tang et al., 1996).--

Please replace the paragraph beginning at page 17, line 27, with the following amended paragraph.

-- The desired cellular location of the molecular pathogenicide, or any components thereof, can be achieved by using the appropriate cellular targeting signals, these include but are not limited to signal peptides, targeting sequences, retention signals, membrane anchors, post translational modifications and/or membrane transmembrane domains that target the protein to the desired organelle, desired membrane (plasma membrane, ER, Golgi, nucleus, chloroplast or vacuole) or desired membrane orientation (cytoplasmic or lumenal or plant cell membrane display) (Kim et al., 1997; Rose and Fink, 1987). Localisation sequences can be targeting sequences which are described, for example in chapter 35 (protein targeting) of L. Stryer *Biochemistry* 4th edition, W.H. Freeman, 1995. Proteins synthesised without a functional signal peptide

are not co-translationally inserted into the secretory pathway and remain in the cytosol. Proteins that carry a signal peptide that directs them to the secretory pathway, which may include a transmembrane sequence or membrane anchor, will be targeted for secretion by default or reside in their target membrane organelles. Targeting signals can direct proteins to the ER, retain them in the ER (LYSLYS motif (SEQ ID NO: 166) and KDEL (SEQ ID NO: 167)), TGN 38, or will target proteins to cell organelles such as the chloroplasts, vacuole, nucleus, nuclear membrane, peroxisomes and mitochondria. Examples for signal sequences and targeting peptides are described in (von Heijne, 1985) (Bennett and Osteryoung, 1991) (Florack et al., 1994). In addition, the targeting signals may be cryptic and encoded by a host plant cell or heterologous eukaryotic cell proteins or animal proteins where the localisation is known and where the protein can be cloned. By constructing a fusion protein with this protein, a molecular pathogenicide can be targeted to the localisation of the protein without the need for identification of the cryptic targeting signal. Suitable cryptic signals are those encoded by the resident Golgi enzymes. --

Please replace the paragraph beginning at page 31, line 15, with the following amended paragraph.

--These and other embodiments are disclosed and encompassed by the description and examples of the present invention. Further literature concerning any one of the methods, uses and compounds to be employed in accordance with the present invention may be retrieved from public libraries, using for example electronic devices. For example the public data base "Medline" may be utilised which is available on the Internet, for example at the following World Wide Web domain site address

"ncbl.nlm.nih.gov/PubMed/medline.html". Further databases and addresses such as those found at the World Wide Web domain site addresses "ncbi.nlm.nih.gov", "infoblogen.fr", A4 "fmi.ch/biology/research_tools.html", and "tigr.org" are known to the person skilled in the art and can also be obtained using search engines such as "lycos.com". An overview of patent information in biotechnology and a survey of relevant sources of patent information useful for retrospective searching and for current awareness if given in Berks, TIBTECH 12 (1994) 352-364.--

Please replace the paragraph beginning at page 32, line 20, with the following amended paragraph.

-- **Figure 3** shows example constructs for molecular pathogenicide display facing the cell cytoplasm. 35SS: 35S promoter from Cauliflower Mosaic Virus with duplicated enhancer; CHS 5'-UT: chalcone synthase 5' A5 untranslated region; VL: Variable domain of the parental monoclonal antibody 24 light chain; VH: Variable domain of the parental monoclonal antibody 24 heavy chain; Linker 1: 14 amino acid linker (Genex 212) sequence; Linker 2: 10 amino acid linker (Gly4Ser)2 sequence (SEQ ID NO: 168); Term: termination sequence from Cauliflower mosaic virus.--

Please replace the paragraph beginning at page 34, line 7, with the following amended paragraph.

--**Figure 7** shows a cDNA construct for targeting and expression of scFv24 on plant cell membranes. CDNAs of mAb24 variable light (V_L) and heavy chain (V_H) domains connected by a 14 amino acid linker were fused to the human TcRβ transmembrane domain and cloned into *EcoRI* and *XbaI* restriction sites of the plant expression vector pSS (33). The DNA sequence of the *EcoRI/XbaI* fragment from pscFv24-TcRβ is depicted in SEQ ID NO:3. 35SS = double enhanced CaMV-35S promoter; CHS-5'-UT = 5' untranslated region of the chalchone synthase; LP = signal sequence of the murine mAb24 light chain; TM = transmembrane domain; TcaMV = CaMV termination sequence.--

Please replace the paragraph beginning at page 36, line 26, with the following amended paragraph.

--**Figure 14** (SEQ ID NO: 19) Molecular pathogenocide based on a single chain (scFv24) fusion to *E. coli* RNAse. The two domains of the pathogenocide were connected by a short Gly-Gly-Gly-Ser (SEQ ID NO: 165) linker peptide. This set up can be modified in multiple ways by using different scFv antibodies binding to structural and nonstructural viral target proteins, other RNAase genes or domains thereof fused to either the N- or C-terminus of any selected scFv cDNA.--

Please replace the paragraph beginning at page 38, line 24 with the following amended paragraph.

--**Figure 21** shows the amino acid residues of two selected scFv binding to the 30K movement protein of TMV obtained by phage display using GST-30K immunized mice for PCR-based amplification of V_H- and V_L- fragments. ScFv 30-1 (SEQ ID NO: 29) = 30K specific scFv No.1, scFv 30 -2 (SEQ ID NO:30) specific scFv No.2. Amino acid residues were derived from cDNA-sequencing of the respective phage derived scFv-cDNA clones as described (Figure 19).--

Please replace the paragraph beginning at page 39, line 4 with the following amended paragraph.

--**Figure 23** shows amino acid sequences derived from the cDNA sequences of antiviral scFv-antibodies obtained by hybridoma rescue (Figure 24) directed against the 3a movement protein of CMV (SEQ ID NO: 113) (23a), a component of the TMV replicase (SEQ ID NO: 114) 23b, 54K of TMV) and a plant virus minimal protein (SEQ ID NO: 115) (23c, 3 min of PLRV).--

Please replace the paragraph beginning at page 39, line 18 with the following amended paragraph.

--**Figure 25**: Epitope mapping of three different antiviral antibodies namely (a) mAb 29 (see Example 1), (b) scFv 54-1 (Example 6,

Figure 23b, Figure 29) and (c) scFv 3a-2 (Example 6, Figure 23a). Sequences were obtained from phage ELISA positive clones after the third round of biopanning using two peptide display libraries (Cortese et al. (1995) Curr. Opin. Biotechno. 6, 73-80). Resulting sequences (SEQ ID NOS: 116-156) were aligned and the consensus epitope was determined. In each case the epitope could be mapped within the parental sequence of the different viral sequences analysed.--

Please replace the Table on pages 68 and 69 with the following amended Table.

--

Name	Specificity according to Kabat (1991)	Overhang/ Enzyme Region	Annealing region
MPD VHF 1 (SEQ ID NO: 31)	Mu V_H IA Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAK GTR CAG CTT CAG GAG TCR GGA
MPD VHF 2 (SEQ ID NO: 32)	Mu V_H IB Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	CAG GTG MAG CTG AWG GAR TCT GG
MPD VHF 3 (SEQ ID NO: 33)	Mu V_H IIA Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAG GTC CAG CTR CAR CAR TCT GGA CC
MPD VHF 4 (SEQ ID NO: 34)	Mu V_H IIA Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	CAG GTW CAG CTS CAG CAG TCT G
MPD VHF 5 (SEQ ID NO: 35)	Mu V_H IIB Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	SAG GTC CAR CTG CAG SAR YCT GGR
MPD VHF 6 (SEQ ID NO: 36)	Mu V_H IIC Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAG GTT CAG CTG CAG CAG TCT GGG
MPD VHF 7 (SEQ ID NO: 37)	Mu V_H IIIA Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAR GTG AAG CTG GTG GAR TCT GGR
MPD VHF 8 (SEQ ID NO: 38)	Mu V_H IIIB Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAG GTG AAG STY MTC GAG TCT GGA
MPD VHF 9	Mu V_H IIIC	C ATG CCA TGA CTC GCG	GAR GTG AAG CTK GAK GAG WCT

Name	Specificity according to Kabat (1991)	Overhang/ Enzyme Region	Annealing region
(SEQ ID NO: 39)	Front	GCC CAG CCG GCC ATG GCC	GR
MPD VHF 10 (SEQ ID NO: 40)	Mu V_H IIID Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAV GTG MWG CTK GTG GAG TCT GGK
MPD VHF 11 (SEQ ID NO: 41)	Mu V_H IIID Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAG GTG CAR CTK GTT GAG TCT GGT G
MPD VHF 12 (SEQ ID NO: 42)	Mu V_H VA Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	SAG GTY CAG CTK CAG CAG TCT GGA
MPD VHF 13 (SEQ ID NO: 43)	Mu V_H 1 Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	CAG ATC CAG TTG GTG CAG TCT GGA
MPD VHF 14 (SEQ ID NO: 44)	Mu V_H 2 Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	CAG GTS CAC STG RWG SAG TCT GGG
MPD VHF 15 (SEQ ID NO: 45)	Mu V_H 3 Front	CAG GTS CAC STG RWG SAG TCT GGG	CAG GTT ACT CTR AAA GWG TST GGC C
MPD VHF 16 (SEQ ID NO: 46)	Mu V_H 4 Front	C ATG CCA TGA CTC GCG GCC CAG CCG GCC ATG GCC	GAT GTG AAC TTG GAA GTG TCT GG
MPD VLF1 (SEQ ID NO: 47)	Mu kappa V_L I Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT GTG MTG WCH CAG TCT CCA
MPD VLF2 (SEQ ID NO: 48)	Mu kappa V_L I Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT CAG ATG ATT CAG TCT CC
MPD VLF3 (SEQ ID NO: 49)	Mu kappa V_L I Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT GTT CTC WHC CAG TCT CC
MPD VLF4 (SEQ ID NO: 50)	Mu kappa V_L I Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT GTG MTG WCH CAG TCT CAA
MPD VLF5 (SEQ ID NO: 51)	Mu kappa V_L II Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAT RTT KTG ATG ACC CAR RCK GCA
MPD VLF6 (SEQ ID NO: 52)	Mu kappa V_L II Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAT RTT KTG ATG ACC CAR RCK CCA
MPD VLF7 (SEQ ID NO: 53)	Mu kappa V_L II Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT GTG ATG ACC CAR BHT G
MPD VLF8 (SEQ ID NO: 54)	Mu kappa V_L II Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAT ATT KTG ATG ACC CAR AYT CC
MPD VLF9 (SEQ ID NO: 55)	Mu kappa V_L III Front	CAT GCC ATG ACT CGC GGC GCG CCT	RAM ATT GTG MTG ACC CAA TYT CCW

Name	Specificity according to Kabat (1991)	Overhang/ Enzyme Region	Annealing region
MPD VLF10 (SEQ ID NO: 56)	Mu kappa V_L IV Front	CAT GCC ATG ACT CGC GGC GCG CCT	SAA AWT GTK CTS ACC CAG TCT CCA
MPD VLF11 (SEQ ID NO: 57)	Mu kappa V_L V/VI Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAY ATY CAG ATG ACM CAG WCT AC
MPD VLF12 (SEQ ID NO: 58)	Mu kappa V_L V/VI Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAY ATY CAG ATG ACH CAG WCT CC
MPD VLF13 (SEQ ID NO: 59)	Mu kappa V_L V/VI Front	CAT GCC ATG ACT CGC GGC GCG CCT	GAC ATT GTG ATG ACT CAG GCT AC
MPD VLF14 (SEQ ID NO: 60)	Mu lambda V_L 1 Front	CAT GCC ATG ACT CGC GGC GCG CCT	CAR SYT GTK STS ACT CAG KAA T
MPD VLF15 (SEQ ID NO: 61)	Mu lambda V_L 1 Front	CAT GCC ATG ACT CGC GGC GCG CCT	CAR SYT GTK STS ACT CAG KCA T
MPD VHB1 (SEQ ID NO: 62)	Mu V_H J_H 1 Back	CTA GTG GTA CTC CAC GGC CGG CCC CTG	MRG AGA CDG TGA SMG TRG TC
MPD VHB2 (SEQ ID NO: 63)	Mu V_H J_H 2 Back	CTA GTG GTA CTC CAC GGC CGG CCC CTG	MRG AGA CDG TGA SRG TRG TG
MPD VHB3 (SEQ ID NO: 64)	Mu V_H J_H 3 Back	CTA GTG GTA CTC CAC GGC CGG CCC CTG	MRG AGA CDG TGA SCA GRG TC
MPD VHB4 (SEQ ID NO: 65)	Mu V_H J_H 4 Back	CTA GTG GTA CTC CAC GGC CGG CCC CTG	MRG AGA CDG TGA STG AGG TT
MPD VHB5 (SEQ ID NO: 66)	Mu V_H J_H 4 Back	CTA GTG GTA CTC CAC GGC CGG CCC CTG	MRG AGA CDG TGA STG ARA TT
MPD VLB1 (SEQ ID NO: 67)	Mu kappa V_L I/II/IV back	CT AGT GGT ACT CCA CGC GGC CGC GTC GAC	AGC MCG TTT CAG YTC CAR YTT
MPD VLB2 (SEQ ID NO: 68)	Mu kappa V_L I/II/IV back	CT AGT GGT ACT CCA CGC GGC CGC GTC GAC	AGC MCG TTT KAT YTC CAR YTT
MPD VLB3 (SEQ ID NO: 69)	Mu kappa V_L IV back	CT AGT GGT ACT CCA CGC GGC CGC GTC GAC	AGC MCG TTT BAK YTC TAT CTT TGT
MPD VLB4 (SEQ ID NO: 70)	Mu kappa V_L I/II/V back	CT AGT GGT ACT CCA CGC GGC CGC GTC GAC	AGC MCG AGC MCG TTT TAT TTC CAA MKT
MPD VLB5 (SEQ ID NO: 71)	Mu lambda V_L back	CT AGT GGT ACT CCA CGC GGC CGC GTC GAC	CTG RCC TAG GAC AGT SAS YTT GGT